

WO 2002049637	A1 20020627	WO 2001-IN221	20011218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
PRIORITY APPLN. INFO.:		IN 2000-MA1085	A 20001218
		IN 2000-MA1086	A 20001218

AB The invention provides a novel **soft gelatin capsule** comprising a fill material consisting essentially of **S-adenosylmethionine (I)** salt disposed within an enteric coated **soft gelatin film**. A capsule contained **I 200**, **stearic acid 84.77**, **gel oil 125**, **dicalcium phosphate 75.0**, **ascorbic acid 1.1**, **anhyd. citric acid 1.1**, **methylparaben 2.2**, **Pr paraben 0.22**, **butylated hydroxy anisole 1.1**, **butylated hydroxy toluene 1.1**, and **soybean oil q.s. 1280 mg.**

IT 57-11-4, **Stearic acid**, biological studies  
 67-63-0, **Isopropyl alcohol**, biological studies  
 75-09-2, **Dichloromethane**, biological studies  
 94-13-3, **Propyl paraben 99-76-3**,  
**Methylparaben 128-37-0**, **Butylated hydroxy toluene**, biological studies 500-38-9,  
**Ndga 9005-65-6**, **Polyoxyethylene sorbitan monooleate 18641-57-1**,  
**Glyceryl behenate 25013-16-5**,  
**Butylated hydroxy anisole 29908-03-0**  
**31566-31-1**, **Glycerylmonostearate 36653-82-4**,  
**Cetyl alcohol**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (soft-gelatin capsule comprising  
 adenosylmethionine)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:425331 HCPLUS  
 DOCUMENT NUMBER: 136:395959  
 TITLE: Antiinflammatory/analgesic method and topical composition including penetration enhancers to treat musculoskeletal disorders  
 INVENTOR(S): Petrus, Edward J.  
 PATENT ASSIGNEE(S): Advanced Medical Instruments, USA  
 SOURCE: U.S., 9 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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=> d 140 ibib abs hitrn 1-27

=> d que stat 140

L2	1 SEA FILE=REGISTRY ABB=ON	29908-03-0
L3	1 SEA FILE=REGISTRY ABB=ON	"S-ADENOSYLMETHIONINE CHLORIDE"/CN
L4	1 SEA FILE=REGISTRY ABB=ON	"S-ADENOSYLMETHIONINE IODIDE"/CN
L5	3 SEA FILE=REGISTRY ABB=ON	L2 OR L3 OR L4
L6	1 SEA FILE=REGISTRY ABB=ON	"STEARIC ACID"/CN
L7	1 SEA FILE=REGISTRY ABB=ON	"CARNUBA WAX"/CN
L8	1 SEA FILE=REGISTRY ABB=ON	BEESWAX/CN
L9	1 SEA FILE=REGISTRY ABB=ON	"POLYOXYETHYLENE SORBITAN MONOOLEATE"/CN
L10	1 SEA FILE=REGISTRY ABB=ON	"CETYL ALCOHOL"/CN
L11	1 SEA FILE=REGISTRY ABB=ON	"GLYCERYL MONOSTEARATE"/CN
L12	1 SEA FILE=REGISTRY ABB=ON	"CETOSTEARYL ALCOHOL"/CN
L13	2 SEA FILE=REGISTRY ABB=ON	"GLYCERYL BEHENATE"/CN
L14	9 SEA FILE=REGISTRY ABB=ON	L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13
L15	1 SEA FILE=REGISTRY ABB=ON	DICHLOROMETHANE/CN
L16	1 SEA FILE=REGISTRY ABB=ON	"ISOPROPYL ALCOHOL"/CN
L17	2 SEA FILE=REGISTRY ABB=ON	L15 OR L16
L18	1 SEA FILE=REGISTRY ABB=ON	"ARACHIS OIL"/CN
L19	1 SEA FILE=REGISTRY ABB=ON	("WHEAT GERM OIL"/CN OR "WHEAT GERM OILS"/CN)
L20	1 SEA FILE=REGISTRY ABB=ON	"CORN OIL"/CN
L21	1 SEA FILE=REGISTRY ABB=ON	"RICE BRAN OIL"/CN
L22	4 SEA FILE=REGISTRY ABB=ON	L18 OR L19 OR L20 OR L21
L23	1 SEA FILE=REGISTRY ABB=ON	NDGA/CN
L24	1 SEA FILE=REGISTRY ABB=ON	"BUTYLATED HYDROXYTOLUENE"/CN
L25	1 SEA FILE=REGISTRY ABB=ON	"BUTYLATED HYDROXYANISOLE"/CN
L26	3 SEA FILE=REGISTRY ABB=ON	L23 OR L24 OR L25
L27	1 SEA FILE=REGISTRY ABB=ON	METHYLPARABEN/CN
L28	1 SEA FILE=REGISTRY ABB=ON	PROPYLPARABEN/CN
L29	2 SEA FILE=REGISTRY ABB=ON	L27 OR L28
L31	1 SEA FILE=HCAPLUS ABB=ON	(L5 OR S(W)ADENOSYLMETHIONINE OR (MONOSULFATE OR MONOSULPHATE OR DISULFATE OR DISULPHATE) (W) TOSYLATE) AND (SOFTGEL OR SOFT(W)GEL)
L33	64 SEA FILE=HCAPLUS ABB=ON	(L5 OR S(W)ADENOSYLMETHIONINE?) AND (?CAPSUL? OR ?DRUG? (W) ?DELIVER?)
L34	8 SEA FILE=HCAPLUS ABB=ON	L33 AND (GEL? OR ?SOFTGEL? OR ?SOFT GEL?)
L35	4 SEA FILE=HCAPLUS ABB=ON	(L5 OR S-ADENOSYLMETHIONINE?) AND (L17 OR DICHLOROMETHAN? OR ISOPROPYL ALCOHOL OR ISOPROPYLALCOHO L OR ISOPROPANOL)
L36	3 SEA FILE=HCAPLUS ABB=ON	(L5 OR S-ADENOSYLMETHIONINE?) AND (L22 OR (SOYA OR SOY OR ARACHIS OR WHEAT(W) GERM OR CORN OR RICE(W) BRAN) (W) OIL)
L37	3 SEA FILE=HCAPLUS ABB=ON	(L5 OR S-ADENOSYLMETHIONINE?) AND (L26 OR NDGA OR (BUTYL? (W) HYDROXY) (W) (TOLUEN? OR ANISOL?))
L38	2 SEA FILE=HCAPLUS ABB=ON	(L5 OR S-ADENOSYLMETHIONINE?) AND (L29 OR (METHYL OR PROPYL) (W) PARABEN OR METHYLPARABEN OR PROPYLPARABEN)
L39	13 SEA FILE=HCAPLUS ABB=ON	(L5 OR S(W)ADENOSYLMETHIONINE?) AND (L14 OR STEARIC ACID OR (CARNUABA OR CARNUBA OR BEE?) (W) WAX OR BEESWAX OR POLYOXYETHYLENE (W) SORBITAN (W) MONOOLEATE? OR (CETYL OR CETOSTEARYL) (W) ALCOHOL? OR GLYCERYL (W) (MONOSTEARAT? OR BEHENAT? OR BEHANAT?))
L40	27 SEA FILE=HCAPLUS ABB=ON	L31 OR L34 OR L35 OR L36 OR L37 OR

L38 OR L39

L40 ANSWER 1 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:595343 HCPLUS  
 DOCUMENT NUMBER: 137:150228  
 TITLE: Antiinflammatory compositions and methods for therapy  
 through enhanced tissue regeneration  
 INVENTOR(S): Uhrich, Kathryn E.; Macedo, Braz  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 17 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002106345	A1	20020808	US 2000-732516	20001207

AB The invention provides methods of promoting healing through enhanced regeneration of tissue (e.g. hard tissue or soft tissue) by contacting the tissue or the surrounding tissue with an antiinflammatory agent, preferably in a controlled-release form, e.g. by dispersing the agent through a polymer matrix, appending the agent to a polymer backbone, or incorporating the agent directly into a biodegradable polymer backbone. These methods are useful in a variety of dental and orthopedic applications. Expts. are presented which demonstrate that implantation of a film comprising an arom. polyanhydride that hydrolyzes to form a therapeutically useful salicylate resulted in less swelling in tissues adjacent to the film and a decrease in the d. of inflammatory cells as compared to other polyanhydride films. Prepn. of e.g. poly[1,6-bis(o-carboxyphenoxy) hexane] is described.

IT 29908-03-0  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (antiinflammatory compns. and methods for therapy through enhanced  
 tissue regeneration)

L40 ANSWER 2 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:487392 HCPLUS  
 DOCUMENT NUMBER: 137:52405  
 TITLE: A novel soft-gelatin  
 capsule comprising S-  
 adenosylmethionine and a method for producing  
 the same  
 INVENTOR(S): Rao, Canakapalli Bhaktavatsala; Chakrabarti, Prasanta  
 Kumar; Ravishankar, Hema  
 PATENT ASSIGNEE(S): Orchid Chemicals and Pharmaceuticals Limited, India  
 SOURCE: PCT Int. Appl., 33 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6399093 B1 20020604 US 1999-314829 19990519  
 AB A method and compn. are disclosed for the treatment of musculoskeletal disorders in mammals by the application of a topical compn. comprising a permeation enhancing amt. of one or more penetration enhancers, and one or more bio-affecting agents to provide anti-inflammatory relief and analgesia to the applied body part.  
 IT 29908-03-0  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antiinflammatotry/analgesic method and topical compn. including penetration enhancers to treat musculoskeletal disorders)  
 IT 94-13-3, Propyl paraben 99-76-3,  
 Methyl paraben  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antiinflammatotry/analgesic method and topical compn. including penetration enhancers to treat musculoskeletal disorders)  
 REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:384295 HCPLUS  
 DOCUMENT NUMBER: 136:390996  
 TITLE: Capsule compositions containing S-adenosyl methionine or its salts  
 INVENTOR(S): Uchida, Yosuke; Miya, Toyofumi; Sato, Koji; Yokoyama, Atsushi; Fukazawa, Takehito; Sugii, Yoshihisa  
 PATENT ASSIGNEE(S): Kohjin Co., Ltd., Japan; Miyako Kagaku Co., Ltd.; Aliment Industry Co., Ltd.  
 SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002145783	A2	20020522	JP 2000-338007	20001106

AB The invention provides a capsule compn. contg. S-adenosyl methionine or its salt as an active ingredient, wherein the S-adenosyl methionine is dispersed in an oily soln., and encapsulated in a gelatin-based capsule shell. A dispersion contg. sunflower oil 60, glycerin fatty acid ester 2.5, beeswax 2.5, and S-adenosyl methionine p-toluenesulfonate disulfate 35 % was encapsulated a gelatin capsule, and tested its storage stability.

IT 29908-03-0  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (capsule compns. contg. S-adenosyl methionine or its salts dispersed in oily solns.)

L40 ANSWER 5 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:903816 HCPLUS  
 DOCUMENT NUMBER: 136:42843  
 TITLE: Compositions, kits, and methods for promoting defined health benefits  
 INVENTOR(S): Kern, Kenneth Norman; Heisey, Matthew Thomas  
 PATENT ASSIGNEE(S): The Procter & Gamble Company, USA

SOURCE: PCT Int. Appl., 45 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1.  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001093847	A2	20011213	WO 2001-US17714	20010601
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-586213	A 20000602
			US 2001-760280	A 20010112

AB The present invention is directed to compns. comprising: (a) a first component selected from the group consisting of gelatin, cartilage, amino sugars, glycosaminoglycans, methylsulfonylmethane, precursors of methylsulfonylmethane, S-adenosylmethionine, salts and mixts.; and (b) a second component comprising a cation source selected from the group consisting of calcium, potassium, magnesium, and mixts. and an edible acid source. The present invention is further directed to food, beverage, pharmaceutical, over-the-counter, and dietary supplement products, which comprise the present compns. The invention also relates to kits comprising the present compns. and information that use of the compn. promotes one or more of the presently defined health benefits, including joint health, bone health, cardiac health, and anti-inflammation. The present invention addnl. relates to methods of treating joint function, bone function, cardiac function, or inflammation comprising administering to a mammal a compn. as defined herein. Thus, hard lemon candies are prep'd. by combining the following components as indicated: sugar 200, light corn syrup 63, water 60, lemon flavor glucosamine-HCl 16, and calcium citrate malate 14.9 g.

IT 29908-03-0  
 RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compns. and kits for promoting defined health benefits)

L40 ANSWER 6 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:903788 HCPLUS  
 DOCUMENT NUMBER: 136:19486  
 TITLE: Kits and methods for optimizing the efficacy of chondroprotective compositions  
 INVENTOR(S): Sarama, Robert Joseph; Harris, Judith Lynn; Spence, Kris Eugene  
 PATENT ASSIGNEE(S): The Procter & Gamble Company, USA  
 SOURCE: PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001093833	A2	20011213	WO 2001-US17721	20010601
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-586514 A 20000602

AB The present invention is directed to kits which are useful for promoting one or more health benefits including, for example, joint health, bone health, cardiac health, and/or anti-inflammation. In particular, the present kits comprise: (a) a compn. comprising one or more chondroprotective agents and water; and (b) information selected from the group consisting of: (i) dose-form information; (ii) instruction or suggestion of ingestion of the compn. within about 4 h of ingestion of a food or beverage; and (iii) combinations thereof. The chondroprotective agent is selected from gelatin, cartilage, amino sugars, glycosaminoglycans, methylsulfonylmethane, precursors of methylsulfonylmethane, S-adenosylmethionine, and their salts. The present invention is further directed to kits comprising: (a) a compn. comprising one or more chondroprotective agents and at least about 80% water; and (b) a sep. food or beverage. The present invention also relates to methods of enhancing a benefit assocd. with a compn. comprising one or more chondroprotective agents and water, the method comprising administering to a mammal the compn. within about 4 h of administration of a food or beverage. For example, a ready-to-drink beverage compn. was prep'd. contg. (by wt.) glucosamine-HCl 3.2%, fructose 9.3%, thickener 0.04%, calcium citrate maleate 2.3%, natural flavors 0.02%, ascorbic acid 0.16%, citric acid 0.35%, and water up to 100%.

IT 29908-03-0

RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(kits and methods for optimizing the efficacy of chondroprotective compns.)

L40 ANSWER 7 OF 27 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:434854 HCPLUS  
DOCUMENT NUMBER: 135:51045  
TITLE: Therapeutic compositions containing anti-inflammatory agents and biodegradable polyanhydrides  
INVENTOR(S): Uhrich, Kathryn; Macedo, Braz  
PATENT ASSIGNEE(S): Rutgers, the State University of New Jersey, USA;  
University of Medicine and Dentistry of New Jersey  
SOURCE: PCT Int. Appl., 40 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041753	A2	20010614	WO 2000-US33378	20001207
WO 2001041753	A3	20020912		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-455861 A 19991207

AB Methods of promoting healing through enhanced regeneration of tissue (e.g. hard tissue or soft tissue) by contacting the tissue or the surrounding tissue with an antiinflammatory agent are useful in a variety of dental and orthopedic applications. Thus, poly[1,6-bis(o-carboxyphenoxy)hexane] was prep'd. in a series of steps by the treatment of salicylic acid with 1,6-dibromohexane, and polymn. of the resulting 1,6-bis(o-carboxyphenoxy)hexane. The polymer was characterized by glass transition temp. measurements and then subjected to compression molding.

IT 29908-03-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (therapeutic compns. contg. antiinflammatory agents and biodegradable polyanhydrides)

L40 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:434848 HCAPLUS  
DOCUMENT NUMBER: 135:51044  
TITLE: Pharmaceutical preparation for treating tumor diseases  
INVENTOR(S): Ghyczy, Miklos; Hager, Joerg; Wendel, Armin  
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer GmbH, Germany  
SOURCE: PCT Int. Appl., 34 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041747	A2	20010614	WO 2000-EP11761	20001125
WO 2001041747	A3	20020207		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19959546	A1	20010621	DE 1999-19959546	19991209
EP 1239862	A2	20020918	EP 2000-979624	20001125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2001021704	A1	20010913	US 2000-731787	20001208

## PRIORITY APPLN. INFO.:

DE 1999-19959546 A 19991209  
WO 2000-EP11761 W 20001125

AB The invention relates to a pharmaceutical prepn. contg. at least one active substance that is cytostatically active, at least one biol. electron acceptor, and the customary pharmaceutical additives. The invention also relates to the use of said prepn. for treating tumor diseases, in particular, for treating cancer. Electron acceptors are betaine, phospholipids, their derivs. etc. Thus 100 g flavopiridol-HCl, 2000 g phosphatidylcholine, 40 g distearoylphosphatidylglycerol, and 250 g betaine linoleate were dispersed in 10 L ethanol; liposomes were formed. The dispersion was added to a soln. of 2 kg maltose in 2 L water, and homogenized. After filtration the dispersion was filled into vials and freeze-dried to yield 100 mg flavopiridol per vial.

IT 57-11-4D, Stearic acid, reaction with betaine

29908-03-0, S-Adenosyl-L-methionine

RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(pharmaceutical prepn. for treating tumor diseases)

L40 ANSWER 9 OF 27 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:161116 HCPLUS

DOCUMENT NUMBER: 132:199074

TITLE: Pharmaceutical and/or diet product

INVENTOR(S): Ghyczy, Miklos; Boros, Mihaly

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 3

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012071	A2	20000309	WO 1999-DE2691	19990827
WO 2000012071	A3	20000615		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19839441	A1	20000302	DE 1998-19839441	19980829
DE 19839443	A1	20000302	DE 1998-19839443	19980829
AU 2000010295	A1	20000321	AU 2000-10295	19990827
			DE 1998-19839441 A	19980829
			DE 1998-19839443 A	19980829
			DE 1999-19919979 A	19990430
			WO 1999-DE2691	W 19990827

## PRIORITY APPLN. INFO.:

AB A pharmaceutical or diet product, esp. for prophylaxis and/or therapy of disorders caused by insufficient O supply, secondary effects of anti-inflammatory active substances, and prophylaxis or therapy of disorders of energy metab., contains .gtoreq.1 compd. having a (CH<sub>2</sub>)<sub>2</sub>N+Me<sub>3</sub> group and/or S-adenosylmethionine. These compds. act

as scavengers for excess electrons produced metabolically during O<sub>2</sub> deficiency and thereby prevent O<sub>2</sub> radical formation and protect against cell damage. Suitable (CH<sub>2</sub>)<sub>2</sub>N+Me<sub>3</sub>-contg. compds. include betaine, acetylcholine, choline, glycerophosphocholine, phosphatidylcholine, lysophosphatidylcholine, carnitine, acylcarnitines, and sphingomyelins. Thus, tablets were prep'd. contg. diclofenac Na 50.0, betaine-HCl 113.64, microcryst. cellulose 30.0, gelatin 3.5, starch 30.86, and Mg stearate 2.0 mg.

IT 29908-03-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical and/or diet product against hypoxia)

L40 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:144082 HCAPLUS  
 DOCUMENT NUMBER: 132:185439  
 TITLE: Oral combination drug containing NSAIDs.  
 INVENTOR(S): Ghyczy, Miklos; Boros, Mihaly  
 PATENT ASSIGNEE(S): Germany  
 SOURCE: Ger. Offen., 8 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19839443	A1	20000302	DE 1998-19839443	19980829
WO 2000012071	A2	20000309	WO 1999-DE2691	19990827
WO 2000012071	A3	20000615		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000010295	A1	20000321	AU 2000-10295	19990827
PRIORITY APPLN. INFO.:			DE 1998-19839441 A	19980829
			DE 1998-19839443 A	19980829
			DE 1999-19919979 A	19990430
			WO 1999-DE2691 W	19990827

AB An oral anti-inflammatory drug combination with minimal side effects contains a NSAID and S-adenosylmethionine and/or a substance contg. a N+Me<sub>3</sub> group (not a surface-active substance), or mixts. thereof. The latter group of compds. protects the gastric epithelium from NSAID-induced gastric ulcers and bleeding. Suitable trimethylammonium compds. include betaine and its derivs., acetylcholine, choline, glycerophosphocholine, carnitine, acetyl-L-carnitine, and sphingomyelin and their mixts. with phosphatidylcholines. Thus, a mixt. of acetylsalicylic acid 80.00, betaine 160.00, microcryst. cellulose 15.00, corn starch 23.25, and stearic acid 1.75 parts was compressed into 175-mg tablets, each contg. 50 mg acetylsalicylic acid. Intragastric administration of 200 mg acetylsalicylic acid into rats

increased the microvascular permeability in the gastric mucosa; this change was reversed by subsequent administration of a fluid contg. 100 mg betaine/kg body wt. and 5% lecithin.

IT 29908-03-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oral combination drug contg. NSAIDs)

L40 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:483380 HCAPLUS

DOCUMENT NUMBER: 131:111442

TITLE: Combinations of tyrosine, methylating agents, phospholipids, fatty acids, and St. John's wort for the treatment of mental disturbances

INVENTOR(S): Henderson, Todd R.; Corson, Barbara E.

PATENT ASSIGNEE(S): Nutramax Laboratories, Inc., USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937155	A1	19990729	WO 1999-US1581	19990126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9924702	A1	19990809	AU 1999-24702	19990126
US 2001033872	A1	20011025	US 2001-862589	20010523
PRIORITY APPLN. INFO.:			US 1998-72721P	P 19980127
			US 1998-75998P	P 19980226
			US 1998-112993P	P 19981218
			US 1999-237222	B1 19990126

AB Therapeutic compns. are provided for the treatment or prevention of mental disturbances such as depressive states and for regulating the level of certain neurotransmitters and thereby improving the function of the central nervous system and cognitive function in humans and other animals. The therapeutic compns. comprise any two or more of tyrosine, one or more methylating agents, one or more phospholipids, one or more fatty acids and St. John's Wort (*Hypericum perforatum*), whether naturally, synthetically, or semi-synthetically derived. Also provided is a method of administering these compns. to humans or animals in need thereof.

IT 57-11-4, Stearic acid, biological studies

29908-03-0, S-Adenosylmethionine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tyrosine, methylating agent, phospholipid, fatty acid, and St. John's wort for treatment of mental disturbance)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 12 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:634375 HCPLUS  
 DOCUMENT NUMBER: 129:312032  
 TITLE: Butylated hydroxytoluene modulates DNA methylation in rats  
 AUTHOR(S): Vanyushin, Boris F.; Lopatina, Nadezhda G.; Wise, Carolyn K.; Fullerton, Floyd R.; Poirier, Lionel A.  
 CORPORATE SOURCE: Division of Molecular Basis of Ontogenesis, A.N. Belozersky Institute of Physico-Chemical Biology, M.V. Lomonosov Moscow State University, Moscow, Russia  
 SOURCE: European Journal of Biochemistry (1998), 256(3), 518-527  
 CODEN: EJBCAI; ISSN: 0014-2956  
 PUBLISHER: Springer-Verlag  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The major observation of this investigation is that a single i.p. injection of butylated hydroxytoluene (BHT, 60 mg/kg body mass) results within a few hours in a strong increase in nuclear DNA(cytosine-5)-Me transferase (Me transferase) activity in the liver, kidneys, heart, spleen, brain and lungs of male rats. In most organs, the rise in Me transferase activity is obsd. as early as 4 h after BHT injection, it reaches a max. at 8 h and then, except for lungs and brain, gradually decreases to its initial level at 16 h. At the max. induction times, the Me transferase activity in liver, kidney and spleen increases by about 16-, 3- and 5-fold, resp. A second BHT injection at 96 h results in a secondary rise in hepatic Me transferase activity. Isoelec. focusing electrophoresis of control rat liver nuclear exts. showed Me transferase activity in the pI 4.7 and 7.4 protein fractions. Both fractions methylate calf thymus DNA better than they do *Drosophila melanogaster* DNA. In similar exts. from BHT-treated rats, the Me transferase activity is found in three protein fractions with pI values equal to 4.0, 6.2 and 9.5, resp. Most of the Me transferase fractions from the livers of BHT-treated rats methylate the completely unmethylated *D. melanogaster* DNA better than they do calf thymus DNA. Thus, BHT induces Me transferase activity that preferably provides de novo DNA methylation. BHT injection had no significant effect on the hepatic contents of **S-adenosylmethionine** (AdoMet), **S-adenosylhomocysteine** (AdoHcy) and AdoMet/AdoHcy ratios. While BHT injection did not alter the 5-methyldeoxycytidine content in liver DNA, it did appear to alter such content in other organs. BHT appears to cause the reversible changes in the methylation status of an internal cytosine residue in some CCGG sites of the rat liver cytosine DNA-Me transferase gene. BHT induces also hypomethylation of the renal Me transferase gene and the hepatic c-Ha-ras gene. While BHT also increases the hepatic mRNA transcripts for the **S-adenosylmethionine synthetase** and the p53 genes, it had no detectable effects on the corresponding mRNA transcripts for Me transferase homologous to murine Me transferase. Thus, BHT induces tissue-specific reversible changes in Me transferase activity and methylation of total DNA and various genes in rats. A strong increase in Me transferase activity in rat liver is accompanied with BHT-induced change in the Me transferase set obsd. in this organ.

IT 128-37-0, BHT, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(butylated hydroxytoluene modulates DNA methylation in rats)  
 IT 29908-03-0, S-Adenosylmethionine  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (liver; butylated hydroxytoluene modulates DNA methylation in rats)

L40 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:613444 HCAPLUS  
 DOCUMENT NUMBER: 129:265466  
 TITLE: Spray formulations of antihyperalgesic opiates and method of treating topical hyperalgesic conditions therewith  
 INVENTOR(S): Maycock, Alan L.; Chang, An-chih; Farrar, John J.; Balogh, Imre  
 PATENT ASSIGNEE(S): Adolor Corp., USA  
 SOURCE: U.S., 8 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811078	A	19980922	US 1997-818559	19970314
US 5798093	A	19980825	US 1997-892389	19970714
PRIORITY APPLN. INFO.:			US 1997-818559	A2 19970314

OTHER SOURCE(S): MARPAT 129:265466

AB Spray formulations of anti-hyperalgesic opiates comprise an anti-hyperalgesic opiate having a peripheral selectivity of 251 to 1,280 in an aq. alc. mixt. contg. up to 15% ethanol, propanol, and/or isopropanol. Thus, 100 g of 4-(p-chlorophenyl)-4-hydroxy-N,N-dimethyl-.alpha.,.alpha.-diphenyl-1-piperidinebutyramide was dissolved in 2 L of a 5 % ethanol/95 % water mixt. with agitation and the soln. was transferred to a pump action spray bottle.

IT 67-63-0, Isopropanol, biological studies

29908-03-0, S-Adenosylmethionine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (topical sprays contg. anti-hyperalgesic opiates and active ingredients to promote wound healing)

L40 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:162631 HCAPLUS  
 DOCUMENT NUMBER: 128:267821  
 TITLE: Investigation of methionine metabolism in peripheral blood mononuclear cells of Irish hyperhomocysteinemic subjects  
 AUTHOR(S): Betts, Vicki; Collins, Patrick B.; Meleady, Raymond; Graham, Ian  
 CORPORATE SOURCE: Department of Biochemistry, Royal College of Surgeons in Ireland, Dublin, 2, Ire.  
 SOURCE: Biochemical Society Transactions (1998), 26(1), S10  
 CODEN: BCSTB5; ISSN: 0300-5127  
 PUBLISHER: Portland Press Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The authors describe a method for the investigation of methionine metab. in peripheral blood mononuclear cells of Irish humans with mild

hyperhomocysteinemia. PMBC of both non- and hyperhomocysteinemic subjects were isolated from whole blood by the method of A. Boyum (Scand. J. Clin. Lab. Invest. 21, 77-99, 1968), cultured in RPMI 1640 media contg. 10% (vol./vol.) fetal calf serum, and 10  $\mu$ g/mL of phytohemagglutinin at a d. of 5 x 10<sup>5</sup> cells/mL at 37°C, in a 5% (vol./vol.) CO<sub>2</sub>/air atm., for 68-72 h. 5  $\mu$ Ci of [35S]-methionine (apprx. 0.05  $\mu$ Ci/nmole) was then added to the cell culture. At various time points the cells were washed and harvested and the enzyme activity was abolished by the addn. of 500  $\mu$ l of ice-cold (100%) ethanol. The ethanol was removed under vacuum and 100  $\mu$ l of a soln. contg. 0.01M perchloric acid and an amino acid mix contg. 0.1  $\mu$ mole each of methionine (met), homocysteine (Hcy), cystathione (Cysta), cysteine (Cys), S-adenosyl homocysteine (SAH) and S-adenosyl methionine (SAM) in 0.1% (vol./vol.) mercaptoethanol was added to the resulting mixt. The cell debris and protein pptd. by this procedure was removed by centrifugation at 5000g for 5 min. The six amino acids were resolved by two-dimensional thin layer chromatog. on cellulose plates, using isopropanol:25 mM phosphate buffer. PH 3.2:formic acid (75:25:6) as the solvent in the first dimension and satd. phenol ammonium hydroxide (31:3) in the second dimension. The position of the amino acids were detd. by staining with ninhydrin. These spots were scraped off the plate into scintillation vials and the radioactivity (counts per min (CPM)) was detd. using 10 mL of scintillant. A metabolite profile was constructed by plotting the percentage of the total radioactivity recovered in each of the major metabolites at various time points. The profile for a hyperhomocysteinemic subject with a genotype indicative of a thermolabile variant of methylenetetrahydrofolate reductase is compared to a control subject.

IT 29908-03-0, S-Adenosyl methionine

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(methionine metab. in peripheral blood mononuclear cells of Irish hyperhomocysteinemic subjects)

L40 ANSWER 15 OF 27 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:694125 HCPLUS

DOCUMENT NUMBER: 126:128585

TITLE: Inhibition of DNA methyltransferase by microbial inhibitors and fatty acids

AUTHOR(S): Suzuki, Kaitarou; Nagao, Kazuhiko; Tokunaga, Jin; Katayama, Naoko; Uyeda, Masaru

CORPORATE SOURCE: Fac. Pharmaceutical Sci., Kumamoto Univ., Kumamoto, 862, Japan

SOURCE: Journal of Enzyme Inhibition (1996), 10(4), 271-280  
CODEN: ENINEG; ISSN: 8755-5093

PUBLISHER: Harwood

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Streptomyces sp. strain No. 560 produces 4 kinds of DNA methyltransferase inhibitors in the culture filtrate. One of them, DMI-4 was distinguished from DMI-1, -2 and -3 previously reported with respect to certain properties. DMI-4 was considered to be a triglyceride consisting of the fatty acids, anteisopentadecanoic acid (C15:0), isopalmitic acid (C16:0), and isostearic acid (C18:0), from the results of gas chromatog. anal. Since DMI-4 contains 3 mols. of fatty acid, and the previously reported DMI-1, 8-methylpentadecanoic acid, is analogous to a fatty acid, the inhibitory activity of various fatty acids and their Me esters was exmd. against DNA methyltransferase EcoRI (M. EcoRI). Oleic acid (C18:1) was

found to be a potent inhibitor of M. EcoRI. The inhibitory activity of oleic acid was shown to be pH- and temp.-dependent and inhibited M. EcoRI in a noncompetitive manner with respect to DNA or **S-adenosylmethionine (SAM)**. The no. of C atoms and double bonds in the fatty acid mol. affected the inhibitory activity, but their Me esters were not inhibitors. The results suggested that the length of the C chain, the no. of double bonds, and the presence of a carboxyl group and branched Me group in the fatty acid mol. may play an important role in the inhibition of DNA methyltransferase.

IT 57-11-4, Octadecanoic acid, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibition of DNA methyltranferases by microbial inhibitors and fatty acids)

L40 ANSWER 16 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:403030 HCPLUS  
 DOCUMENT NUMBER: 121:3030  
 TITLE: Experimental databases on inhibition of the bacterial mutagenicity of 4-nitroquinoline 1-oxide and cigarette smoke  
 AUTHOR(S): Camoirano, Anna; Balansky, Roumen M.; Bennicelli, Carlo; Izzotti, Alberto; D'Agostini, Francesco; De Flora, Silvio  
 CORPORATE SOURCE: Inst. Hygiene, Univ. Genoa, Genoa, I-16132, Italy  
 SOURCE: Mutation Research (1994), 317(2), 89-109  
 CODEN: MUREAV; ISSN: 0027-5107  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Two antimutagenicity databases were prep'd. by applying a co-treatment procedure to the *Salmonella* reversion assay. Ninety compds. belonging to various chem. classes were quant. tested for antimutagenicity towards the direct-acting mutagen 4-nitroquinoline 1-oxide (4NQO) in strain TA100 of *S. typhimurium* and 63 of them were addnl. tested for antimutagenicity towards unfractionated mainstream cigarette smoke (CS) in strain TA98, in the presence of S9 mix. Twelve compds. (13.3%) inhibited 4NQO mutagenicity by at least 50%, with a MID50 (dose inhibiting 50% of mutagenicity) varying over a 1226-fold range. Twenty-six compds. (41.3%) inhibited CS mutagenicity, with a MID50 varying over a 520-fold range. Three compds. only, i.e., bilirubin, curcumin and myricetin, were capable of inhibiting the mutagenicities of both 4NQO and CS. However, myricetin and the other flavonoid rutin were at the same time mutagenic by inducing frameshift mutations following metabolic activation. There was a rather rigorous selectivity of antimutagenicity data depending on the chem. class of inhibitors and it was possible to discriminate protective effects within several pairs or series of structurally related compds. For instance, all eight thiols and aminothiols inhibited 4NQO mutagenicity, which contrasted with the inactivity of the remaining 17 sulfur compds. tested, all of them lacking a free sulphydryl group. The mutagenicity of CS was consistently inhibited by the majority of phenols (eight out of 10 tested) and by all two isothiocyanates, two dithiocarbamates, three indole derivs., three tetrapyrrole compds. and three flavonoids tested. Although the results obtained cannot be extrapolated to other mutagens or test systems, they may provide a useful source of information for research in the area of antimutagenesis and for the development of chemopreventive agents.

IT 128-37-0, Bht, biological studies 25013-16-5, Bha  
 29908-03-0, S-Adenosylmethionine

RL: BIOL (Biological study)  
 (exptl. databases on inhibition of bacterial mutagenicity of  
 nitroquinoline oxide and cigarette smoke in relation to)

L40 ANSWER 17 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:73099 HCPLUS  
 DOCUMENT NUMBER: 120:73099  
 TITLE: Nod factor production by Azorhizobium caulinodans  
 strain ORS571  
 AUTHOR(S): Holsters, M.; Geelen, D.; Goethal, K.; Van Montagu,  
 M.; Geremia, R.; Prome, J. C.; Mergaert, P.  
 CORPORATE SOURCE: Lab. Genet., Univ. Gent, Ghent, B-9000, Belg.  
 SOURCE: Current Plant Science and Biotechnology in Agriculture  
 (1993), 17(New Horizons in Nitrogen Fixation), 191-6  
 CODEN: CPBAE2; ISSN: 0924-1949

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Although Azorhizobium is taxonomically rather divergent from Rhizobium and Bradyrhizobium, it does harbor several similar nod genes and thus it came as no surprise that upon induction of nod gene expression, lipo-oligosaccharide Nod factors were found secreted in the culture medium. The NodARc factors are chitin tetramers or pentamers N-acylated at the non-reducing end with either vaccenic or stearic acid and carrying several unusual substitutions. Part of the pentamers are branched at the reducing end with D-arabinose. The non-reducing end is substituted with an N-Me group in all mols. and a carbamoyl group on part of the pentamers and all of the tetramers. NodARc factors cause morphol. changes on Sesbania rostrata roots: induction of both root hair formation and meristematic foci at lateral root bases, the sites where upon bacterial infection the root nodules are formed. Some of the azorhizobial nod genes can be implied in Nod factor synthesis. The nodS gene most likely encodes a S-adenosylmethionine-dependent methyltransferase for Nod factor methylation. A gene nolK may be involved in the synthesis of an arabinosyl precursor for factor glycosylation at the reducing end; the NolK-deduced polypeptide has a NAD/NADP-binding motif and shows similarity to NAD/NADP-requiring sugar epimerases.

L40 ANSWER 18 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1993:142293 HCPLUS  
 DOCUMENT NUMBER: 118:142293  
 TITLE: Purification of a 40-kilodalton methyltransferase  
 active in the aflatoxin biosynthetic pathway  
 AUTHOR(S): Keller, N. P.; Dischinger, H. C., Jr.; Bhatnagar, D.;  
 Cleveland, T. E.; Ullah, A. H. J.  
 CORPORATE SOURCE: Southern Reg. Res. Cent., U.S. Dep. Agric., New  
 Orleans, LA, 70179, USA  
 SOURCE: Applied and Environmental Microbiology (1993), 59(2),  
 479-84  
 CODEN: AEMIDF; ISSN: 0099-2240

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The penultimate step in the aflatoxin biosynthetic pathway of the filamentous fungi Aspergillus flavus and A. parasiticus involves conversion of sterigmatocystin to O-methylsterigmatocystin. An S-adenosylmethionine-dependent sterigmatocystin methyltransferase that catalyzes this reaction was purified to homogeneity (>90%) from 78-h-old mycelia of A. parasiticus SRR 163. The purifn. of this sol.

enzyme was carried out by 5 soft-gel chromatog. steps: cell debris remover treatment, QMA ACELL chromatog., hydroxylapatite-Ultrogel chromatog., DEAE-Spheredex chromatog., and octyl-Avidgel chromatog., followed by MA7Q HPLC. SDS-PAGE of the protein peak from this step with Ag staining identified a single band with a mol. wt. of .apprx.40 kDa. This purified protein was distinct from a dimeric 168-kDa methyltransferase previously purified from the same fungal strain under identical growth conditions. The chromatog. behavior and N-terminal sequence of the 40-kDa enzyme were also distinct from those of the 168-kDa methyltransferase. The molar extinction coeff. of the 40-kDa enzyme at 278 nm was estd. to be 4.7 .times. 104 M<sup>-1</sup> cm<sup>-1</sup> in 50 mM K phosphate buffer (pH 7.5).

IT 29908-03-0, S-Adenosyl-L-methionine

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with sterigmatocystin methyltransferase of Aspergillus parasiticus, kinetics of)

L40 ANSWER 19 OF 27 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:149365 HCPLUS

DOCUMENT NUMBER: 116:149365

TITLE: Characterization of membrane fraction lipid composition and function of cirrhotic rat liver. Role of S-adenosyl-L-methionine

AUTHOR(S): Muriel, Pablo; Mourelle, Marisabel

CORPORATE SOURCE: Dep. Farmacol. Toxicol., IPN, Mexico City, Mex.

SOURCE: Journal of Hepatology (1992), 14(1), 16-21

CODEN: JOHEEC; ISSN: 0168-8278

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of S-adenosyl-L-methionine (SAM) administration on the lipid compn. of the membrane fraction obtained from livers of cirrhotic rats was studied. Four groups of animals were used: group 1 received CCl<sub>4</sub> for 8 wk to induce cirrhosis. Animals in group 2 received 3 daily i.m. injections of SAM 20 mg/kg in addn. to CCl<sub>4</sub>. Groups 3 and 4 were control groups of SAM and vehicles. Seventy-two h after the end of treatment all animals were killed and livers were studied to measure glycogen, cAMP contents and to isolate membrane fractions. The membrane activity of Na<sup>+</sup>,K<sup>+</sup>- and Ca<sup>2+</sup>-ATPases was measured and the lipid content was analyzed in exts. Phospholipids were detd. by TLC and fatty acids by GC. Chronic CCl<sub>4</sub> treatment led to increases in cholesterol and in the cholesterol/phospholipid ratio. Anal. of phospholipids revealed an increase in phosphatidylserines. Satd. fatty acids increased, while unsatd. decreased. The CCl<sub>4</sub>-treated group showed a decrease in glycogen and an increase in cAMP contents. Na<sup>+</sup>,K<sup>+</sup>- and Ca<sup>2+</sup>-ATPases activity were highly reduced in cirrhotic membranes. In the group receiving CCl<sub>4</sub> + SAM the lipid compn. and the function of liver membrane fraction showed no difference compared to normal controls, except for fatty acid compn. which was similar to concns. in the CCl<sub>4</sub>-treated group. Glycogen depletion was only partially prevented whereas cAMP levels were normalized in the CCl<sub>4</sub> + SAM group. The results showed that membrane lipid alterations were accompanied by changes in the activity of enzymes embedded in the membrane fraction derived from CCl<sub>4</sub>-cirrhotic rats. The beneficial effects of SAM treatment obsd. in cirrhotic rats, demonstrated the importance of biol. transmethylation in preserving the lipid compn. of hepatocyte membranes and in maintaining the normal function of the liver.

IT 57-11-4, Stearic acid, biological studies

RL: BIOL (Biological study)  
(of hepatocyte cell membrane fractions, in cirrhosis, adenosyl

methionine effect on)

IT 29908-03-0, S-Adenosyl-L-methionine  
 RL: BIOL (Biological study)  
 (phospholipid compn. of hepatocyte cell membrane fractions response to,  
 in cirrhosis)

L40 ANSWER 20 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:532467 HCPLUS  
 DOCUMENT NUMBER: 115:132467  
 TITLE: Membrane fluidity and membrane lipid composition in  
 rat liver sinusoidal and canalicular membrane vesicles  
 AUTHOR(S): Kurumi, Yoshiaki  
 CORPORATE SOURCE: Sch. Med., Kinki Univ., Osaka, Japan  
 SOURCE: Kinki Daigaku Igaku Zasshi (1991), 16(1), 139-48  
 CODEN: KDIZDD; ISSN: 0385-8367  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese  
 AB Membrane fluidity and phospholipid compn. of sinusoidal membrane vesicles  
 (SMV) and canalicular membrane vesicles (CMV) of rat hepatocytes were  
 studied to investigate their relevance to the topol. difference in  
 membrane function. Membrane fluidity was measured by fluorescence  
 polarization of 1,6-diphenyl-1,3,5-hexatrien (DPH) and by the spin label  
 method using 5-doxyl stearic acid (5-DSA) and 16-doxyl  
 stearic acid (16-DSA) as probes. Fluidity of CMV was  
 lower than that of SMV in the both methods. CMV had a higher total  
 phospholipid content than SMV. Phospholipid compn. was detd. by a newly  
 developed HPLC method. The level of sphingomyelin was higher and the  
 level of phosphatidylcholine lower in CMV than SMV. The cholesterol level  
 was higher in CMV than in SMV. These alterations of lipid compn. in CMV  
 are considered to be related to the decrease in fluidity. Addn. of  
 S-adenosyl-L-methionine (SAM), which is reported to improve cholestasis,  
 to SMV resulted in an increase in fluidity and Na<sup>+</sup>,K<sup>+</sup>-ATPase activity.  
 These changes may contribute to the choleretic effect of SAM.

IT 29908-03-0, S-Adenosyl-L-methionine  
 RL: BIOL (Biological study)  
 (fluidity of membranes of liver sinusoid response to, phospholipid  
 compn. in relation to)

L40 ANSWER 21 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:191788 HCPLUS  
 DOCUMENT NUMBER: 114:191788  
 TITLE: Selenium biomethylation in an alkaline, saline  
 environment  
 AUTHOR(S): Thompson-Eagle, E. T.; Frankenberger, W. T., Jr.  
 CORPORATE SOURCE: Dep. Soil and Environ. Sci., Univ. California,  
 Riverside, CA, 92521, USA  
 SOURCE: Water Research (1991), 25(2), 231-40  
 CODEN: WATRAG; ISSN: 0043-1354  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Biomethylation of Se in evapn. pond water was studied and optimized in  
 lab.-incubated mesocosms. Methylating microorganisms, present in all pond  
 waters collected from the San Joaquin Valley, California, were inhibited  
 by bactericides (10 mg/L crystal violet, 100 mg/L penicillin G, and a 1:1  
 mixt. of 50 mg/L penicillin G and 50 mg/L polymyxin B sulfate), but not by  
 fungicides (100 mg/L cycloheximide; 200 mg/L nystatin and 50 mg/L sodium  
 dichromate). The addn. of casein (4 g/L) increased bacterial nos.  
 10000-fold and stimulated biomethylation 26-fold. The provision of growth

matrixes (sand, glass beads or nylon polymers) stimulated Se biomethylation in unamended water but not in peptone-amended water. Biomethylation was optimal in a well-mixed, aerobic system amended with a protein source. Cofactors (10. $\mu$ M homocysteine and 10. $\mu$ M reduced glutathione) enhanced the prodn. of Me<sub>2</sub>Se in peptone-amended pond water. The species of inorg. Se present, SeO<sub>3</sub><sup>2-</sup> and SeO<sub>4</sub><sup>2-</sup>, had little effect on the methylation efficiency. Increasing the Se concn. to 1.9, 3.9, 11.9, 21.9, or 101.9 mg Se/L in peptone-amended pond water decreased the percentage of Se removed from 8 to 3.8, 2, 1.3, 0.7, and 0.1%, resp. Selenium removal ranged from 8 to 100% for peptone-amended pond waters contg. between 2.2 and 0.02 . $\mu$ g Se/L, resp. Biomethylation was inhibited by 0.1M NO<sub>3</sub><sup>-</sup> and NO<sub>2</sub><sup>-</sup>, but addnl. SO<sub>4</sub><sup>2-</sup> (0.1, 1M) had no effect on DMSe release. It may be possible to apply these findings to the design of a bioreactor to deselenify agricultural drainage water.

IT 29908-03-0, **S-Adenosylmethionine**

RL: PROC (Process)

(di-Me selenide formation by aquatic microorganisms in presence of, in evapn. pond waters in San Joaquin Valley, California)

L40 ANSWER 22 OF 27 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1989:19646 HCPLUS

DOCUMENT NUMBER: 110:19646

TITLE: 1,2-Dimethylhydrazine-induced premalignant alterations in the **S-adenosylmethionine** /S-adenosylhomocysteine ratio and membrane lipid lateral diffusion of the rat distal colon

AUTHOR(S): Halline, Allan G.; Dudeja, Pradeep K.; Brasitus, Thomas A.

CORPORATE SOURCE: Dep. Med., Univ. Chicago, Chicago, IL, USA

SOURCE: Biochim. Biophys. Acta (1988), 944(1), 101-7

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Male rats were s.c. injected with dimethylhydrazine (20 mg/kg/wk) or diluent for 5 wk. Animals from each group were killed, distal colonic tissue harvested and the levels of **S-adenosylmethionine**, **S-adenosylhomocysteine**, and decarboxylated **S-adenosylmethionine** measured by HPLC. The activity of methionine adenosyltransferase was also examd. in these tissues. Addnl., brush-border membranes were isolated from the distal colonocytes of control and treated animals and examd. and compared with respect to their phospholipid methylation activities as well as their lipid fluidity as assessed by the rotational mobilities of the probes 1,6-diphenyl-1,3,5-hexatriene and DL-12-(9-anthroyl)stearic acid and translational mobility of the fluorophore pyrenedecanoic acid. The results of these studies demonstrated: (1) phospholipid methyltransferase activity in rat colonic plasma membranes was increased concomitantly with increases in the cellular levels of **S-adenosylmethionine** and the **S-adenosylmethionine/S-adenosylhomocysteine** ratio in the distal colonic segment of treated-animals; and (2) the lateral diffusion of rat distal colonic brush-border membrane lipids, as assessed by the ratio of excimer/monomer fluorescence intensities of the fluorophore pyrenedecanoate, was also increased after dimethylhydrazine administration to these animals for 5 wk.

IT 29908-03-0, **S-Adenosylmethionine**

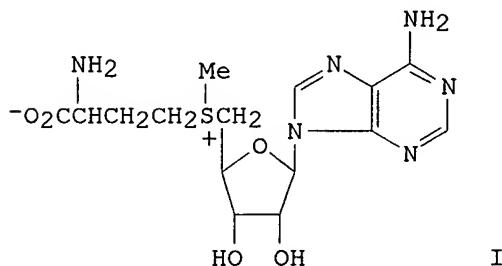
RL: BIOL (Biological study)

(of distal colon, dimethylhydrazine effect on)

L40 ANSWER 23 OF 27 HCPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1983:443517 HCPLUS  
 DOCUMENT NUMBER: 99:43517  
 TITLE: Preparation and stabilization of S-adenosyl-L-methionine  
 PATENT ASSIGNEE(S): Kanegafuchi Chemical Industry Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58049397	A2	19830323	JP 1981-148103	19810918

GI



AB Anticholesteremic S-adenosyl-L-methionine (I) [29908-03-0] is prep'd. and stabilized by org. acids and Mg salts. Thus, 360 g baker's yeast was extd. with 1.8 L 1.5 N HClO<sub>4</sub>, and the ext. was subjected to column chromatog. contg. acidic cation exchanger Dowex 50WX8, eluted with H<sub>2</sub>SO<sub>4</sub>, passed through a column contg. activated C, eluted with H<sub>2</sub>SO<sub>4</sub> followed by a H<sub>2</sub>SO<sub>4</sub>-MeOH mixt., the eluate concd., treated with MeOH to produce a white pptd., 4.8 g I sulfate [69673-08-1], which was isolated and dried. I sulfate in the presence of butyric acid [107-92-6] and MgSO<sub>4</sub> was stable.

IT 57-11-4, biological studies

RL: BIOL (Biological study)  
 (adenosylmethionine stabilization by magnesium sulfate and)

IT 29908-03-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and stabilization of)

L40 ANSWER 24 OF 27 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:194627 HCPLUS  
 DOCUMENT NUMBER: 98:194627  
 TITLE: Stabilization of hydrolysis prone labile organic reagents in liquid media  
 INVENTOR(S): Modrovich, Ivan  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 722,565, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 8  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4372874	A	19830208	US 1980-206467	19801113
US 4153511	A	19790508	US 1977-764826	19770202
US 4310624	A	19820112	US 1977-775833	19770309
AT 43917	E	19890615	AT 1979-102058	19790621
PRIORITY APPLN. INFO.:			US 1976-667857	19760317
			US 1976-722565	19760913
			US 1977-764826	19770202
			US 1977-775833	19770309
			US 1978-919159	19780626
			EP 1979-102058	19790621

AB A labile, org. reagent, which is unstable in aq. media and stable in a nonaq. media, is stabilized by dissolving the org. reagent in a water-miscible, org. solvent which is liq. at room temp. and which is nondegradatively reactive with the org. reagent to form a soln. of the org. reagent in the org. solvent. At least 1% of an inert, high-surface area particulate desiccant is added to the soln. for entrapping water with the desiccant so that the residual water content of the soln. is <0.5%. The desiccant can be removed from the soln. before sealing it. More than 1 org. reagent can be added to the solvent, and a solubilizing agent for the org. reagent can be used. The title method is esp. applicable to coenzymes, as well as other org. compds. For example, NAD was dissolved in H<sub>2</sub>O-free ethylene glycol. The soln. was stable at 25.degree. for 6-12 mo. and at 4-8.degree. for 2-4 yr.

IT 67-63-0, uses and miscellaneous

RL: USES (Uses)  
 (as solvent, in org. reagents stabilization)

IT 29908-03-0

RL: PROC (Process)  
 (stabilization of)

L40 ANSWER 25 OF 27 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1982:436754 HCPLUS

DOCUMENT NUMBER: 97:36754

TITLE: Stimulation of fatty acid methylation in human red cell membranes by phospholipase A2 activation

AUTHOR(S): Engelsen, Steinar J.; Zatz, Martin

CORPORATE SOURCE: Lab. Clin. Sci., Natl. Inst. Mental Health, Bethesda, MD, 20205, USA

SOURCE: Biochim. Biophys. Acta (1982), 711(3), 515-20

CODEN: BBACAO; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nonpolar methylated products comprise .apprx.50% of the radioactive material extractable into CHCl<sub>3</sub>-MeOH after incubation of human red cell membranes with S-[methyl-3H]adenosylmethionine. One of these nonpolar products is fatty acid Me ester. The enzyme which synthesizes fatty acid Me ester had an apparent Km for **S-adenosylmethionine** of .apprx.0.6 .mu.M and a Vmax of .apprx.0.6 pmol/mg protein/30 min. Half-maximal activity was achieved upon addn. of .apprx.20 .mu.M Na oleate. Of the fatty acids tested, Na oleate increased most effectively

(6-fold) and arachidonic acid was ineffective. Evidence indicated that fatty acid methylation takes place on the cytoplasmic side of the plasma membrane. The reaction was demonstrable in intact cells incubated with [methyl-3H]methionine and increased upon addn. of Na oleate. Incubation of intact cells with melittin, a potent membrane phospholipase A2 activator from bee venom, increased fatty acid methylation several-fold. Fatty acid methylation appears to be one of the consequences of phospholipase A2 action in plasma membranes.

IT 57-11-4, biological studies

RL: BIOL (Biological study)

(fatty acid methylation by human erythrocyte in response to)

IT 29908-03-0

RL: RCT (Reactant)

(reaction of, with human fatty acid methylase, kinetics of)

L40 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1978:485586 HCAPLUS

DOCUMENT NUMBER: 89:85586

TITLE:

Ornithine and S-adenosylmethionine

decarboxylases in mouse epidermal cell cultures  
treated with tumor promoters

AUTHOR(S):

Lichti, Ulrike; Yuspa, Stuart H.; Hennings, Henry

CORPORATE SOURCE:

Div. Cancer Cause Prev., Natl. Cancer Inst., Bethesda,  
Md., USA

SOURCE:

Carcinog. - Compr. Surv. (1978), 2 (Mech. Tumor Promot.  
Cocarcinog.), 221-32

CODEN: CCSUDL; ISSN: 0145-0158

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Mouse epidermal cell cultures were treated with tumor promoters to det. the mechanism of action of these compds. by measuring ornithine decarboxylase (ODC) [9024-60-6] stimulation. 12-O-tetradecanoylphorbol 13-acetate (I) [16561-29-8] and other phorbol deriv. dose-dependently stimulated ODC in relation to their in vivo tumorigenic activity and in vivo and in vitro DNA synthesis stimulating activity. Several Tweens also stimulated ODC activity, but with poor correlation to tumor-promoting activity. Several other compds. with known or suspected promoting activity only slightly stimulated ODC. I unexpectedly inhibited S-adenosylmethionine decarboxylase [9036-20-8], possibly the cause for the onset of I stimulation of DNA synthesis in vitro.

IT 9005-65-6

RL: BIOL (Biological study)

(ornithine decarboxylate of epidermal cell cultures response to, carcinogenicity in relation to)

L40 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1975:138191 HCAPLUS

DOCUMENT NUMBER: 82:138191

TITLE:

Dietary induction of hepatic microsomal enzymes by thermally oxidized fats

AUTHOR(S):

Andia, Ana M.; Street, Joseph C.

CORPORATE SOURCE:

Dep. Chem. Biochem., Utah State Univ., Logan, Utah,  
USA

SOURCE:

J. Agric. Food Chem. (1975), 23(2), 173-7

CODEN: JAFCAU

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Functional changes assocd. with the hepatomegaly commonly obsd. upon

feeding thermally oxidized (TO) fats were investigated. Rats were fed purified diets in which the fat consisted of fresh **corn oil**, TO oil, or the proportional amt. of nonurea adduct-forming material (NUAF) from TO oil plus fresh oil. Increases in relative liver wts. and the concns. of microsomal protein and endogenous malondialdehyde were obsd. when TO oil or NUAF plus fresh oil were fed rather than pure fresh oil with 2 types of dietary protein, casein and soybean. Both the basal and DDT-induced mixed function oxidase activities were higher in animals fed TO oil and NUAF than in those given fresh oil. The TO oil also increased cytochrome P-450 and the activity of **S-adenosylmethionine:phosphatidylethanolamine methyltransferase** whereas the NUAF did not. Oxidized fat thus appears to stimulate smooth endoplasmic reticulum proliferation and induce a complex of microsomal enzymes.

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=> d que stat 142
L2      1 SEA FILE=REGISTRY ABB=ON 29908-03-0
L3      1 SEA FILE=REGISTRY ABB=ON "S-ADENOSYLMETHIONINE CHLORIDE"/CN
L4      1 SEA FILE=REGISTRY ABB=ON "S-ADENOSYLMETHIONINE IODIDE"/CN
L5      3 SEA FILE=REGISTRY ABB=ON L2 OR L3 OR L4
L6      1 SEA FILE=REGISTRY ABB=ON "STEARIC ACID"/CN
L7      1 SEA FILE=REGISTRY ABB=ON "CARNUBA WAX"/CN
L8      1 SEA FILE=REGISTRY ABB=ON BEESWAX/CN
L9      1 SEA FILE=REGISTRY ABB=ON "POLYOXYETHYLENE SORBITAN MONOOLEATE"/CN
L10     1 SEA FILE=REGISTRY ABB=ON "CETYL ALCOHOL"/CN
L11     1 SEA FILE=REGISTRY ABB=ON "GLYCERYL MONOSTEARATE"/CN
L12     1 SEA FILE=REGISTRY ABB=ON "CETOSTEARYL ALCOHOL"/CN
L13     2 SEA FILE=REGISTRY ABB=ON "GLYCERYL BEHENATE"/CN
L14     9 SEA FILE=REGISTRY ABB=ON L6 OR L7 OR L8 OR L9 OR L10 OR L11
          OR L12 OR L13
L15     1 SEA FILE=REGISTRY ABB=ON DICHLOROMETHANE/CN
L16     1 SEA FILE=REGISTRY ABB=ON "ISOPROPYL ALCOHOL"/CN
L17     2 SEA FILE=REGISTRY ABB=ON L15 OR L16
L18     1 SEA FILE=REGISTRY ABB=ON "ARACHIS OIL"/CN
L19     1 SEA FILE=REGISTRY ABB=ON ("WHEAT GERM OIL"/CN OR "WHEAT GERM
          OILS"/CN)
L20     1 SEA FILE=REGISTRY ABB=ON "CORN OIL"/CN
L21     1 SEA FILE=REGISTRY ABB=ON "RICE BRAN OIL"/CN
L22     4 SEA FILE=REGISTRY ABB=ON L18 OR L19 OR L20 OR L21
L23     1 SEA FILE=REGISTRY ABB=ON NDGA/CN
L24     1 SEA FILE=REGISTRY ABB=ON "BUTYLATED HYDROXYTOLUENE"/CN
L25     1 SEA FILE=REGISTRY ABB=ON "BUTYLATED HYDROXYANISOLE"/CN
L26     3 SEA FILE=REGISTRY ABB=ON L23 OR L24 OR L25
L27     1 SEA FILE=REGISTRY ABB=ON METHYLPARABEN/CN
L28     1 SEA FILE=REGISTRY ABB=ON PROPYLPARABEN/CN
L29     2 SEA FILE=REGISTRY ABB=ON L27 OR L28
L31     1 SEA FILE=HCAPLUS ABB=ON (L5 OR S(W)ADENOSYLMETHIONINE OR
          (MONOSULFATE OR MONOSULPHATE OR DISULFATE OR DISULPHATE) (W)TOSY
          LATE) AND (SOFTGEL OR SOFT(W)GEL)
L33     64 SEA FILE=HCAPLUS ABB=ON (L5 OR S(W)ADENOSYLMETHIONINE?) AND
          (?CAPSUL? OR ?DRUG? (W) ?DELIVER?)
L34     8 SEA FILE=HCAPLUS ABB=ON L33 AND (GEL? OR ?SOFTGEL? OR ?SOFT
          GEL?)
L35     4 SEA FILE=HCAPLUS ABB=ON (L5 OR S-ADENOSYLMETHIONINE?) AND
          (L17 OR DICHLOROMETHAN? OR ISOPROPYL ALCOHOL OR ISOPROPYLALCOHO
          L OR ISOPROPANOL)
L36     3 SEA FILE=HCAPLUS ABB=ON (L5 OR S-ADENOSYLMETHIONINE?) AND
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(L22 OR (SOYA OR SOY OR ARACHIS OR WHEAT (W) GERM OR CORN OR RICE (W) BRAN) (W) OIL)  
 L37 3 SEA FILE=HCAPLUS ABB=ON (L5 OR S-ADENOSYLMETHIONINE?) AND (L26 OR NDGA OR (BUTYL? (W) HYDROXY) (W) (TOLUEN? OR ANISOL?))  
 L38 2 SEA FILE=HCAPLUS ABB=ON (L5 OR S-ADENOSYLMETHIONINE?) AND (L29 OR (METHYL OR PROPYL) (W) PARABEN OR METHYLPARABEN OR PROPYLPARABEN)  
 L39 13 SEA FILE=HCAPLUS ABB=ON (L5 OR S (W) ADENOSYLMETHIONINE?) AND (L14 OR STEARIC ACID OR (CARNUABA OR CARNUBA OR BEE?) (W) WAX OR BEESWAX OR POLYOXYETHYLENE (W) SORBITAN (W) MONOOLEATE? OR (CETYL OR CETOSTEARYL) (W) ALCOHOL? OR GLYCERYL (W) (MONOSTEARAT? OR BEHENAT? OR BEHANAT?))  
 L40 27 SEA FILE=HCAPLUS ABB=ON L31 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39  
 L41 21 SEA L40  
 L42 16 DUP REMOVE L41 (5 DUPLICATES REMOVED)

=> d ibib abs 1-16

L42 ANSWER 1 OF 16 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2002-315281 [35] WPIDS  
 DOC. NO. CPI: C2002-091709  
 TITLE: Polymer useful in medical therapy for treating e.g. cancer comprises a backbone containing ester, thioester or amide linkages and a group yielding a biologically active compound.  
 DERWENT CLASS: A23 A96 B05 B07 C03  
 INVENTOR(S): UHRICH, K E  
 PATENT ASSIGNEE(S): (UHRI-I) UHRICH K E; (RUTF) UNIV RUTGERS STATE NEW JERSEY  
 COUNTRY COUNT: 96  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002009768	A2	20020207 (200235)*	EN	51	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ					
NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK					
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR					
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU					
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001078055	A	20020213 (200238)			
US 2002071822	A1	20020613 (200243)			

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002009768	A2	WO 2001-US23747	20010727
AU 2001078055	A	AU 2001-78055	20010727
US 2002071822	Provisional	US 2000-220707P	20000727
	Provisional	US 2001-261337P	20010112
		US 2001-917194	20010727

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
-----		
AU 2001078055 A	Based on	WO 200209768
PRIORITY APPLN. INFO: US 2001-261337P 20010112; US 2000-220707P 20000727; US 2001-917194 20010727		
AN 2002-315281 [35]	WPIDS	
AB WO 200209768 A	UPAB: 20020603	
NOVELTY - A polymer comprises a backbone containing ester, thioester or amide linkages and at least one group which will yield a biologically active compound on hydrolysis of the polymer.		
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:		
(a) a biocompatible and bio-degradable polyester or polyamide comprising the biologically active compound containing at least 2 alcohol or phenol groups or at least two amine groups co-polymerized to bis(acyl) chlorides or carboxylic acids;		
(b) producing the biocompatible and bio-degradable polyester or polyamide by co-polymerizing the biologically active compound with carboxylic acid groups or bis(acyl) chlorides; and		
(c) delivering the biologically active compound to a host by administering the biocompatible and bio-degradable polyester or polyamide.		
ACTIVITY - Cytostatic; Antipsoriatic; Dermatological; Anti-inflammatory; Analgesic; Antiparkinsonian; Antithrombotic; Antibacterial; Fungicide; Immunosuppressive.		
No details of tests showing activity are given.		
MECHANISM OF ACTION - None given in the source material.		
USE - In medical therapy for the manufacture of a medicament for treating diseases e.g. cancer, psoriasis, inflammatory bowel disease, skin cancers, brain tumor, pain or Parkinson's disease in mammals preferably humans; and useful as they have anti-bacterial, antiinflammatory, antifungal, antithrombotic and immunosuppressive activities (all claimed). Also useful in dental and cosmetic applications, in medical implant applications to form shaped articles such as vascular grafts and stents, bone plates, sutures, implantable sensors, implantable drug delivery devices, stents for tissue regeneration and other articles that decompose into non-toxic components within known time period. In oral formulations and products e.g. skin moisturizers, cleaners, pads plasters, lotions, creams, gels, ointments, solutions, shampoos, tanning products and lipsticks.		
ADVANTAGE - The polymers can be readily processed into pastes or solvent cast to yield films coatings, microspheres and fibres with different geometric shapes for design of various medical implants and may also be processed by compression molding and extrusion.		
Dwg.0/0		
L42 ANSWER 2 OF 16	WPIDS (C) 2002 THOMSON DERWENT	
ACCESSION NUMBER:	2002-329425 [36]	WPIDS
DOC. NO. CPI:	C2002-095110	
TITLE:	Polymers useful in medical therapy for treating e.g. cancer comprises a backbone containing an anhydride linkage and a group yielding a biologically active compound.	
DERWENT CLASS:	A28 A96 B05 B07 C03	
INVENTOR(S):	UHRICH, K E	
PATENT ASSIGNEE(S):	(UHRI-I) UHRICH K E; (RUTF) UNIV RUTGERS STATE NEW JERSEY	
COUNTRY COUNT:	96	
PATENT INFORMATION:		

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2002009767 A2	20020207 (200236)*	EN	38		
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ					
NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK					
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR					
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU					
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001078052 A 20020213 (200238)					

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002009767 A2		WO 2001-US23740	20010727
AU 2001078052 A		AU 2001-78052	20010727

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001078052 A	Based on	WO 200209767

PRIORITY APPLN. INFO: US 2000-627215 20000727

AN 2002-329425 [36] WPIDS

AB WO 200209767 A UPAB: 20020610

NOVELTY - A polymer comprises a backbone containing an anhydride linkage and at least one group which will yield a biological compound (A) on hydrolysis of the polymer. (A) is not an ortho-hydroxy aryl carboxylic acid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (a) a pharmaceutical composition comprising (A) and a carrier;
- (b) producing a biocompatible and biodegradable polyester or polyamide which degrades into (A). The method involves co-polymerizing (A) containing at least 2 alcohol or phenol groups or at least 2 amine groups with carboxylic acid groups or bis(acyl)chlorides; and
- (c) delivering (A) to a host by administering the biocompatible and biodegradable polyester or polyamide to the host.

ACTIVITY - Antibacterial; Antifungal; Cytostatic; Antiinflammatory; Immunosuppressive.

MECHANISM OF ACTION - None given.

USE - In medical therapy of the manufacture of a medicament for treating diseases e.g. cancer in mammals preferably humans (all claimed), in polymeric **drug delivery** systems containing low molecular weight drugs, in medical, dental and cosmetic applications as vascular grafts and stents, bone plates, sutures, implantable sensors, implantable **drug delivery** devices, stents for tissue regeneration and other articles that decompose into non-toxic components within a known time period. The polymers can also be incorporated into oral formulations and products such as skin moisturizers, cleansers, pads, plasters, lotions, creams, **gels**, ointments, solutions, shampoos, tanning products and lipsticks.

ADVANTAGE - The polymers have enhanced solubility and processability as well as degradation properties. The polymers can be readily processed into pastes or solvent cast to yield films, coatings, microspheres and

fibers with different geometric shapes of design of various medical implants and may also be processed by compression molding and extrusion.  
Dwg.0/0

L42 ANSWER 3 OF 16 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2002-602515 [65] WPIDS  
 DOC. NO. CPI: C2002-170599  
 TITLE: Capsule formulation for use as health food or pharmaceuticals, contains liquid containing **S-adenosylmethionine** or its salt, dispersed or suspended in oil solution, and sealed in **gelatin capsule**.  
 DERWENT CLASS: B02 B07  
 PATENT ASSIGNEE(S): (ARIM-N) ARIMENTO KOGYO KK; (KOJK) KOHJIN CO LTD;  
 (MIYA-N) MIYAKO KAGAKU KK  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2002145783 A		20020522 (200265)*			6

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2002145783 A		JP 2000-338007	20001106

PRIORITY APPLN. INFO: JP 2000-338007 20001106

AN 2002-602515 [65] WPIDS

AB JP2002145783 A UPAB: 20021010

NOVELTY - A **capsule** formulation contains liquid containing **S-adenosylmethionine** or its salt, dispersed or suspended in the oil solution. The resulting suspension is sealed in a **gelatin capsule**.

ACTIVITY - Antidepressant; antiarthritic; hepatotropic. No test details are given for the above mentioned activity.

MECHANISM OF ACTION - None given.

USE - For producing **S-adenosylmethionine** or its salt, containing **capsule** formulation which is used as health food or pharmaceutical product. **S-adenosylmethionine** or its salt, improves depression, arthritis, liver disease (liver cirrhosis).

ADVANTAGE - **S-adenosylmethionine** or its salt is easily dispersed in edible oil. The **capsule** formulation is stable as the **capsule** outer layer hinders the absorption of atmospheric moisture content by **S-adenosylmethionine** or its salt (which is hydroscopic).

Dwg.0/0

L42 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 2001:296447 BIOSIS  
 DOCUMENT NUMBER: PREV200100296447  
 TITLE: Glycine N-methyltransferase is up-regulated by all-trans- and 13-cis-retinoic acid in rats.  
 AUTHOR(S): Rowling, Matthew J. (1); Schalinske, Kevin L. (1)  
 CORPORATE SOURCE: (1) Food Science and Human Nutrition, Iowa State

SOURCE: University, Ames, IA, 50011 USA  
 FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A602.  
 print.  
 Meeting Info.: Annual Meeting of the Federation of American  
 Societies for Experimental Biology on Experimental Biology  
 2001 Orlando, Florida, USA March 31-April 04, 2001  
 ISSN: 0892-6638.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Glycine N-methyltransferase (GNMT) functions to regulate **s-adenosylmethionine** (SAM) levels and the ratio of SAM/**S-adenosylhomocysteine** (SAH). SAM is a universal methyl group donor and up-regulation of GNMT may lead to wastage of methyl groups required for transmethylation reactions. Previous work in our laboratory demonstrated that dietary treatment of rats with 13-cis-retinoic acid (13-CRA) decreased the hepatic concentration of SAM and the ratio of SAM/SAH. In this study, we examined the ability of 13-CRA, as well as all-trans-retinoic acid (ATRA), to regulate hepatic GNMT as a potential basis for our earlier observations. Male Sprague Dawley rats were fed either a control (10% casein + 0.3% methionine) diet or a control diet supplemented with 1% methionine (MS diet). Following a 5-day acclimation period, an equal number of rats from each dietary group were orally given either ATRA, 13-CRA (both @ 30  $\mu$ mol/kg body weight), or vehicle (corn oil) daily for 10 days. For rats fed the control diet, administration of both 13-CRA and ATRA elevated the hepatic GNMT activity 1.5- (0.256 nmol/min mg protein) and 1.3-fold (0.230 nmol/min mg protein), respectively, compared to the control (vehicle-treated) group (0.172 nmol/min mg protein). Similar results were exhibited by rats fed the MS diet. Moreover, the retinoid-induced elevations in enzymatic activity were reflected in the abundance of GNMT protein. As expected, hepatic SAM levels and the SAM/SAH ratio decreased concomitantly with an increase in GNMT activity. These data suggest that the up-regulation of GNMT by retinoid administration may be due to the induction of GNMT protein production. To our knowledge, this is the first report of a compound that induces GNMT activity at the transcriptional and/or translational level.

L42 ANSWER 5 OF 16 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-059906 [05] WPIDS

DOC. NO. CPI: C1999-017742

TITLE: Non watery low alcohol sake - contains ethyl caproate, **isopropyl alcohol**, n-propanol and isobutanol.

DERWENT CLASS: D16

INVENTOR(S): ASAHI, A; BOU, M; MORISHITA, Y

PATENT ASSIGNEE(S): (ASAHI) ASAHI KASEI KOGYO KK

COUNTRY COUNT: 3

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9855592	A1	19981210	(199905)*	JA	42
		W: AU US			
JP 11046751	A	19990223	(199918)		14
AU 9870787	A	19981221	(199919)		
JP 3035592	B2	20000424	(200025)		14

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9855592	A1	WO 1998-JP1833	19980422
JP 11046751	A	JP 1998-117874	19980414
AU 9870787	A	AU 1998-70787	19980422
JP 3035592	B2	JP 1998-117874	19980414

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9870787	A Based on	WO 9855592
JP 3035592	B2 Previous Publ.	JP 11046751

PRIORITY APPLN. INFO: JP 1997-160681 19970604

AN 1999-059906 [05] WPIDS

AB WO 9855592 A UPAB: 19990203

Low alcohol sake contains 4-12% ethanol with a sake-meter of -50 to -25 and acidity of 1.5-4, 0.05-10 ppm ethyl caproate, at least 90 ppm isopropyl alcohol, at least 60 ppm n-propanol, at least 40 ppm isobutanol and sustaining the characteristic sake flavour.

The ethanol content is preferably 6-9 with sake-meter of -45 to -30 and acidity of 2-4. The sake contains 0.05-10 (preferably 0.05-3) ppm ethyl caproate, 0.01-1 (preferably 0.01-0.3) ppm ethyl caprylate, 0.05-10 (preferably 0.05-3) ppm isoamyl acetate, 2-10 (preferably 2-10) ppm acetaldehyde, 0.002-0.05 (preferably 0.002-0.01) ppm isobutyraldehyde, 0.001-0.05 (preferably 0.001-0.01) ppm isovaleraldehyde, 15-90 (preferably 15-50) ppm isoamyl alcohol, 10-60 (preferably 10-40) ppm n-propanol and 4-40 (preferably 4-20) isobutanol. The pyruvic acid concentration is at least 90 (particularly at least 40) ppm with at least 30 (particularly at least 0.2) mM total of S-adenosylmethionine and methylthioadenosine. The sake is brewed from cereals, koji (malt), water and yeast.

ADVANTAGE - The sake is not watery and has balanced sour and sweet tastes and sustained characteristics of sake flavour and aroma.

Dwg.0/0

L42 ANSWER 6 OF 16 MEDLINE DUPLICATE 1  
 ACCESSION NUMBER: 1998451507 MEDLINE  
 DOCUMENT NUMBER: 98451507 PubMed ID: 9780227  
 TITLE: Butylated hydroxytoluene modulates DNA methylation in rats.  
 AUTHOR: Vanyushin B F; Lopatina N G; Wise C K; Fullerton F R;  
 Poirier L A  
 CORPORATE SOURCE: Division of Molecular Basis of Ontogenesis, A.N. Belozersky  
 Institute of Physico-Chemical Biology, M.V. Lomonosov  
 Moscow State University, Russia..  
 Vanyushin@moo.genebee.msu.su  
 SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1998 Sep 15) 256 (3)  
 518-27.  
 Journal code: 0107600. ISSN: 0014-2956.  
 PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199811  
 ENTRY DATE: Entered STN: 19990106

Last Updated on STN: 19990106  
 Entered Medline: 19981105

AB The major observation of this investigation is that a single intraperitoneal injection of butylated hydroxytoluene (BHT, 60 mg/kg body mass) results within a few hours in a strong increase in nuclear DNA(cytosine-5)-methyl transferase (methyl transferase) activity in the liver, kidneys, heart, spleen, brain and lungs of male rats. In most organs, the rise in methyl transferase activity is observed as early as 4 h after BHT injection, it reaches a maximum at 8 h and then, except for lungs and brain, gradually decreases to its initial level at 16 h. At the maximum induction times, the methyl transferase activity in liver, kidney and spleen increases by about 16-, 3- and 5-fold, respectively. A second BHT injection at 96 h results in a secondary rise in hepatic methyl transferase activity. Isoelectric focusing electrophoresis of control rat liver nuclear extracts showed methyl transferase activity in the pI 4.7 and 7.4 protein fractions. Both fractions methylate calf thymus DNA better than they do *Drosophila melanogaster* DNA. In similar extracts from BHT-treated rats, the methyl transferase activity is found in three protein fractions with pI values equal to 4.0, 6.2 and 9.5, respectively. Most of the methyl transferase fractions from the livers of BHT-treated rats methylate the completely unmethylated *D. melanogaster* DNA better than they do calf thymus DNA. Thus, BHT induces methyl transferase activity that preferably provides de novo DNA methylation. BHT injection had no significant effect on the hepatic contents of **S-adenosylmethionine** (AdoMet), **S-adenosylhomocysteine** (AdoHcy) and AdoMet/AdoHcy ratios. While BHT injection did not alter the 5-methyldeoxycytidine content in liver DNA, it did appear to alter such content in other organs. BHT appears to cause the reversible changes in the methylation status of an internal cytosine residue in some CCGG sites of the rat liver cytosine DNA-methyl transferase gene. BHT induces also hypomethylation of the renal methyl transferase gene and the hepatic c-Ha-ras gene. While BHT also increases the hepatic mRNA transcripts for the **S-adenosylmethionine** synthetase and the p53 genes, it had no detectable effects on the corresponding mRNA transcripts for methyl transferase homologous to murine methyl transferase. Thus, BHT induces tissue-specific reversible changes in methyl transferase activity and methylation of total DNA and various genes in rats. A strong increase in methyl transferase activity in rat liver is accompanied with BHT-induced change in the methyl transferase set observed in this organ.

L42 ANSWER 7 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 96157008 EMBASE  
 DOCUMENT NUMBER: 1996157008  
 TITLE: Nutrition and bile formation.  
 AUTHOR: Tuchweber B.; Yousef I.M.; Ferland G.; Perea A.  
 CORPORATE SOURCE: Departement de Nutrition, Universite de Montreal, 2405  
 chemin Cote Sainte-Catherine, Montreal, Que. H3T 1A8, Canada  
 SOURCE: Nutrition Research, (1996) 16/6 (1041-1080).  
 ISSN: 0271-5317 CODEN: NTRSDC  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 029 Clinical Biochemistry  
 048 Gastroenterology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB This review summarizes current knowledge on mechanisms involved in hepatic bile formation and the role of diet as a modulator of this important liver function. It also includes cholestasis and nutritional interventions known

to exert a beneficial effect in this pathology. Two components of the bile flow have been described: bile acid dependent (BADF) and bile acid independent (BAIF) flows and, several cellular structures are known to be involved in their generation. The membrane's enzyme activities, transporters and pumps play a particularly important role in bile secretion. Of the macronutrients, dietary protein has been shown to markedly affect bile flow. Protein deficient diet results in a decrease of both BADF and BAIDF, and in increased susceptibility to bile acid (BA)-induced cholestasis. Amino acid mixtures included in TPN solutions as well as certain individual amino acids can induce cholestasis mainly through alterations of plasma membrane composition and function. Supplementation with taurine and S-adenosyl methionine prevents these forms of cholestasis by maintaining membrane integrity and function. The quantity and quality of dietary lipid influences bile secretion. Enhanced bile flow was observed with high polyunsaturated fat intake and was attributed to both higher BADF and BAIDF. Diets enriched in fish oil were found to result in the generation of greater bile flow when compared to diets enriched in corn oil. Dietary phospholipid (soybean lecithin) supplementation increases bile secretion and exerts a beneficial effect against BA-induced cholestasis probably by maintenance of membrane integrity. Although there is much information on the role of dietary carbohydrates, fibers, minerals and vitamins on cholesterol and BA metabolism, relatively little is known about their implication in bile formation. Finally certain dietary strategies such as energy restriction and starve-refeed regimen can enhance bile secretion by their effects on BADF and BAIDF through maintenance of membrane function. In conclusion, diet is an important modulator of bile formation and secretion by affecting BA synthesis and metabolism as well as membrane structure and function.

L42 ANSWER 8 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 94272996 EMBASE  
 DOCUMENT NUMBER: 1994272996  
 TITLE: Heterologous expression of the *bchM* gene product from *Rhodobacter capsulatus* and demonstration that it encodes S-adenosyl-L-methionine:Mg- protoporphyrin IX methyltransferase.  
 AUTHOR: Bollivar D.W.; Jiang Z.-Y.; Bauer C.E.; Beale S.I.  
 CORPORATE SOURCE: Division of Biology and Medicine, Brown University, Providence, RI 02912, United States  
 SOURCE: *Journal of Bacteriology*, (1994) 176/17 (5290-5296).  
 ISSN: 0021-9193 CODEN: JOBAAY  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB The bacteriochlorophyll biosynthesis gene, *bchM*, from *Rhodobacter capsulatus* was previously believed to code for a polypeptide involved in formation of the cyclopentone ring of protochlorophyllide from Mg- protoporphyrin IX monomethyl ester. In this study, *R. capsulatus* *bchM* was expressed in *Escherichia coli* and the gene product was subsequently demonstrated by enzymatic analysis to catalyze methylation of Mg- protoporphyrin IX to form Mg-protoporphyrin IX monomethyl ester. Activity required the substrates Mg-protoporphyrin IX and S-adenosyl-L-methionine. <sup>14</sup>C-labeled product was formed in incubations containing <sup>14</sup>C-methyl- labeled S-adenosyl-L-methionine. On the basis of these and previous results, we also conclude that the *bchH* gene, which was

previously reported to code for Mg-protoporphyrin IX methyltransferase, is most likely involved in the Mg chelation step.

L42 ANSWER 9 OF 16 MEDLINE DUPLICATE 2  
 ACCESSION NUMBER: 93167811 MEDLINE  
 DOCUMENT NUMBER: 93167811 PubMed ID: 8434913  
 TITLE: Purification of a 40-kilodalton methyltransferase active in the aflatoxin biosynthetic pathway.  
 AUTHOR: Keller N P; Dischinger H C Jr; Bhatnagar D; Cleveland T E; Ullah A H  
 CORPORATE SOURCE: Southern Regional Research Center, Agricultural Research Service, U.S. Department of Agriculture, New Orleans, Louisiana 70179.  
 SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (1993 Feb) 59 (2) 479-84.  
 Journal code: 7605801. ISSN: 0099-2240.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199303  
 ENTRY DATE: Entered STN: 19930402  
 Last Updated on STN: 19930402  
 Entered Medline: 19930317

AB The penultimate step in the aflatoxin biosynthetic pathway of the filamentous fungi *Aspergillus flavus* and *A. parasiticus* involves conversion of sterigmatocystin to O-methylsterigmatocystin. An *s*-adenosylmethionine-dependent methyltransferase that catalyzes this reaction was purified to homogeneity (> 90%) from 78-h-old mycelia of *A. parasiticus* SRRC 163. Purification of this soluble enzyme was carried out by five soft-gel chromatographic steps: cell debris removal treatment, QMA ACELL chromatography, hydroxylapatite-Ultrogel chromatography, DEAE-Spheredex chromatography, and Octyl Avidgel chromatography, followed by MA7Q high-performance liquid chromatography. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of the protein peak from this step on silver staining identified a single band of approximately 40 kDa. This purified protein was distinct from the dimeric 168-kDa methyltransferase purified from the same fungal strain under identical growth conditions (D. Bhatnagar, A. H. J. Ullah, and T. E. Cleveland, Prep. Biochem. 18:321-349, 1988). The chromatographic behavior and N-terminal sequence of the 40-kDa enzyme were also distinct from those of the 168-kDa methyltransferase. The molar extinction coefficient of the 40-kDa enzyme at 278 nm was estimated to be  $4.7 \times 10(4)$  M<sup>-1</sup> cm<sup>-1</sup> in 50 mM potassium phosphate buffer (pH 7.5).

L42 ANSWER 10 OF 16 MEDLINE  
 ACCESSION NUMBER: 92325007 MEDLINE  
 DOCUMENT NUMBER: 92325007 PubMed ID: 1624419  
 TITLE: Methylation of FrzCD, a methyl-accepting taxis protein of *Myxococcus xanthus*, is correlated with factors affecting cell behavior.  
 AUTHOR: McBride M J; Kohler T; Zusman D R  
 CORPORATE SOURCE: Department of Molecular and Cell Biology, University of California, Berkeley 94720.  
 CONTRACT NUMBER: 1 F32 GM12356-01A1 (NIGMS)  
 GM20509 (NIGMS)  
 SOURCE: JOURNAL OF BACTERIOLOGY, (1992 Jul) 174 (13) 4246-57.  
 Journal code: 2985120R. ISSN: 0021-9193.

PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199208  
 ENTRY DATE: Entered STN: 19920821  
 Last Updated on STN: 19970203  
 Entered Medline: 19920807

AB Myxococcus xanthus, a nonflagellated gliding bacterium, exhibits multicellular behavior during vegetative growth and fruiting body formation. The frizzy (frz) genes are required to control directed motility for these interactions. The frz genes encode proteins that are homologous to all of the major enteric chemotaxis proteins, with the exception of CheZ. In this study, we characterized FrzCD, a protein which is homologous to the methyl-accepting chemotaxis proteins from the enteric bacteria. FrzCD, unlike the other methyl-accepting chemotaxis proteins, was found to be localized primarily in the cytoplasmic fraction of cells. FrzCD migrates as a ladder of bands on sodium dodecyl sulfate-polyacrylamide gel electrophoresis, reflecting heterogeneity due to methylation or demethylation and to deamidation. FrzCD was shown to be methylated in vivo when cells were exposed to yeast extract or Casitone and demethylated when starved in buffer. We used the methylation state of FrzCD as revealed by Western blot (immunoblot) analyses to search for stimuli that are recognized by the frz signal transduction system. Common amino acids, nucleotides, vitamins, and sugars were not recognized, but certain lipids and alcohols were recognized. For example, the saturated fatty acids capric acid and lauric acid stimulated FrzCD methylation, whereas a variety of other saturated fatty acids did not. Lauryl alcohol and lipoic acid also stimulated methylation, as did phospholipids containing lauric acid. In contrast, several short-chain alcohols, such as isoamyl alcohol, and some other solvents caused demethylation. The relatively high concentrations of the chemicals required for a response may indicate that these chemicals are not the relevant signals recognized by *M. xanthus* in nature. Isoamyl alcohol and isopropanol also had profound effects on the behavior of wild-type cells, causing them to reverse continuously. Cells of frzB, frzF, and frzG mutants also reversed continuously in the presence of isoamyl alcohol, whereas cells of frzA, frzCD, or frzE mutants did not. On the basis of the data presented, we propose a model for the frz signal transduction pathway in *M. xanthus*.

L42 ANSWER 11 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 91347922 EMBASE  
 DOCUMENT NUMBER: 1991347922  
 TITLE: Diet and toxicity of chemicals.  
 AUTHOR: Rogers A.E.  
 CORPORATE SOURCE: Department of Pathology, Mallory Institute of Pathology, Boston University School of Medicine, 80 E. Concord Street, Boston, MA, United States  
 SOURCE: Journal of Nutritional Biochemistry, (1991) 2/11 (579-593).  
 ISSN: 0955-2863 CODEN: JNBIEL  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 016 Cancer  
 029 Clinical Biochemistry  
 052 Toxicology  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English

SUMMARY LANGUAGE: English

AB Nutrient and non-nutrient diet components influence the biological activity of many chemicals in different ways and by different mechanisms. The most intensive investigation has focused on interactions between diet and chemical carcinogenicity, and some general metabolic interactions have been elucidated that are applicable to groups of chemicals or diet components. Similar interactions are known for noncarcinogenic chemicals and for drugs. In most cases, however, present knowledge consists of observed phenomena without mechanisms or explanations. These cases present opportunities for research that will permit greater understanding and generalization of results.

L42 ANSWER 12 OF 16 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 88326968 MEDLINE  
 DOCUMENT NUMBER: 88326968 PubMed ID: 3415996  
 TITLE: 1,2-Dimethylhydrazine-induced premalignant alterations in the **S-adenosylmethionine** /S-adenosylhomocysteine ratio and membrane lipid lateral diffusion of the rat distal colon.  
 AUTHOR: Halline A G; Dudeja P K; Brasitus T A  
 CORPORATE SOURCE: Department of Medicine, University of Chicago, IL.  
 CONTRACT NUMBER: CA 36745 (NCI)  
 SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1988 Sep 15) 944 (1) 101-7.  
 Journal code: 0217513. ISSN: 0006-3002.  
 PUB. COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198810  
 ENTRY DATE: Entered STN: 19900308  
 Last Updated on STN: 19980206  
 Entered Medline: 19881027

AB Prior studies by our laboratory, utilizing the 1,2-dimethylhydrazine experimental model of colonic cancer, had shown that administration of this procarcinogen for 5 weeks was found to increase phospholipid methyltransferase activity and the fluidity of rat distal colonic brush-border membranes. The present studies were conducted to further explore these 'premalignant' colonic phenomena. Male albino rats of the Sherman strain were subcutaneously injected with dimethylhydrazine (20 mg/kg body weight per week) or diluent for 5 weeks. Animals from each group were killed, distal colonic tissue harvested and the levels of **S-adenosylmethionine**, **S-adenosylhomocysteine** and decarboxylated **S-adenosylmethionine** measured by high performance liquid chromatography. The activity of methionine adenosyltransferase was also examined in these tissues. Additionally, brush-border membranes were isolated from the distal colonocytes of control and treated-animals and examined and compared with respect to their phospholipid methylation activities as well as their lipid fluidity as assessed by the rotational mobilities of the probes 1,6-diphenyl-1,3,5-hexatriene and DL-12-(9-anthroyl)**stearic acid** and translational mobility of the fluorophore pyrenedecanoic acid. The results of these studies demonstrated: (1) phospholipid methyltransferase activity in rat colonic plasma membranes was increased concomitantly with increases in the cellular levels of **S-adenosylmethionine** and the **S-adenosylmethionine** /S-adenosylhomocysteine ratio in the distal colonic segment of treated-animals; and (2) the lateral diffusion of rat distal colonic brush-border membrane lipids, as assessed by the ratio of excimer/monomer

fluorescence intensities of the fluorophore pyrenedecanoate, was also increased after dimethylhydrazine administration to these animals for 5 weeks.

L42 ANSWER 13 OF 16 MEDLINE  
 ACCESSION NUMBER: 87184598 MEDLINE  
 DOCUMENT NUMBER: 87184598 PubMed ID: 3105533  
 TITLE: Activation of polyamine biosynthetic decarboxylases during the acute phase response of rat liver.  
 AUTHOR: Scalabrino G; Ferioli M E; Piccoletti R; Bernelli-Zazzera A  
 SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1987 Mar 30) 143 (3) 856-62.  
 Journal code: 0372516. ISSN: 0006-291X.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198705  
 ENTRY DATE: Entered STN: 19900303  
 Last Updated on STN: 19980206  
 Entered Medline: 19870518

AB The activities of ornithine decarboxylase and *s-adenosylmethionine* decarboxylase increase in the livers of rats during the acute-phase response to inflammation. The increase reaches its maximum at 2.5 hr from injection of turpentine, and is maintained at the same level for the following 2 days. Pretreatment *in vivo* with an inhibitor of cyclooxygenase prevents the inflammation-associated increases of both polyamine biosynthetic decarboxylases: an inhibitor of the lipoxygenase pathway seems to counteract only the increase of ornithine decarboxylase. The administration of diaminopropane, an inhibitor of ornithine decarboxylase, has only limited effects on the activation of RNA synthesis by liver nuclei, which occurs 10 hr after turpentine treatment. The results suggest that stimulation of the polyamine biosynthetic decarboxylases is surely part of the acute-phase response and depends on the previous activation of arachidonate metabolism: however its role in supporting later events of the acute-phase response will need further investigations.

L42 ANSWER 14 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 88113448 EMBASE  
 DOCUMENT NUMBER: 1988113448  
 TITLE: Study of factors influencing the *in vivo* methylation of inorganic arsenic in rats.  
 AUTHOR: Buchet J.P.; Lauwerys R.  
 CORPORATE SOURCE: Industrial Toxicology and Occupational Health Unit, University of Louvain, 1200 Brussels, Belgium  
 SOURCE: Toxicology and Applied Pharmacology, (1987) 91/1 (65-74). ISSN: 0041-008X CODEN: TXAPA  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal  
 FILE SEGMENT: 035 Occupational Health and Industrial Medicine  
 052 Toxicology  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Previous studies have shown that several factors may influence the methylation of inorganic arsenic by rat liver *in vitro* (Buchet and

Lauwerys, 1985). The present study attempts to assess the relevance of these observations *in vivo*. Like man, rat inactivates inorganic arsenic by methylation to monomethylarsonic (MMA) and dimethylarsinic (DMA) acids which are excreted in urine along with unchanged inorganic arsenic (Asi). The administration of S-adenosylmethionine alone or in association with reduced (GSH) or oxidized glutathione or acetylcysteine and the increase of hepatic GSH level by butylated hydroxytoluene pretreatment do not stimulate the urinary excretion of the methylated arsenic metabolites following a challenge dose of inorganic arsenic. Conversely a reduction of the hepatic GSH level by phorone pretreatment greatly modifies the metabolism of inorganic arsenic *in vivo*. A reduction exceeding 90% of the control value leads to a decreased urinary excretion of MMA and DMA and an increased urinary excretion of inorganic arsenic. This is also associated with an increased accumulation of inorganic arsenic in the liver. This suggests that a drastic reduction of GSH level in liver not only impairs the methylation of inorganic arsenic but also impairs its biliary excretion. When GSH depletion is less severe, the total amount of arsenic excreted in urine after a challenge dose of NaAsO<sub>2</sub> is not significantly different from that found in unpretreated animals but the proportion of the three metabolic forms is different: MMA is reduced whereas Asi and DMA tend to increase. These changes resemble those found in patients with liver insufficiency (J.P. Buchet, A. Geubel, S. Pauwels, P. Mahieu, and R. Lauwerys (1984). The influence of liver disease on the methylation of arsenite in humans. (Arch. Toxicol. 55, 151-154). Long-term pretreatment of rats with CCl<sub>4</sub> slightly reduces the amount of MMA and DMA excreted in urine following a challenge dose of inorganic arsenic. This effect may result from a reduction of GSH transferase activity by CCl<sub>4</sub>. This study demonstrates the important role of liver GSH in the metabolism of inorganic arsenic *in vivo*.

L42 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1980:82420 BIOSIS

DOCUMENT NUMBER: BR19:19918

TITLE: BIOSYNTHESIS OF METHYLATED NONPOLAR LIPIDS INCLUDING FATTY-ACID METHYL ESTERS BY RAT LUNG MEMBRANES.

AUTHOR(S): ZATZ M; DUDLEY P A; MARKEY S P

CORPORATE SOURCE: LAB. CLIN. SCI., NATL. INST. MENT. HEALTH, BUILD. 10 ROOM 2D47, BETHESDA, MD. 20205, USA.

SOURCE: 71ST ANNUAL MEETING OF THE AM. SOC. BIOL. CHEM. HELD WITH THE BIOPHYS. SOC., NEW ORLEANS, LA., USA, JUNE 1-6, 1980. FED PROC, (1980) 39 (6), ABSTRACT 223.

CODEN: FEPRA7. ISSN: 0014-9446.

DOCUMENT TYPE: Conference

FILE SEGMENT: BR; OLD

LANGUAGE: English

L42 ANSWER 16 OF 16 JAPIO COPYRIGHT 2002 JPO

ACCESSION NUMBER: 2002-145783 JAPIO

TITLE: ENCAPSULATED PHARMACEUTICAL PREPARATION CONTAINING S-ADENOSYLMETHIONINE OR ITS SALTS

INVENTOR: UCHIDA YOSUKE; MIYA TOYOFUMI; SATO KOJI; YOKOYAMA ATSUSHI; FUKAZAWA TAKEHITO; SUGII YOSHIHISA

PATENT ASSIGNEE(S): KOHJIN CO LTD  
MIYAKO KAGAKU CO LTD  
ARIMENTO KOGYO KK

PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 2002145783	A	20020522	Heisei	A61K031-7076

## APPLICATION INFORMATION

STN FORMAT: JP 2000-338007 20001106  
ORIGINAL: JP2000338007 Heisei  
PRIORITY APPLN. INFO.: JP 2000-338007 20001106  
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2002

AN 2002-145783 JAPIO

AB PROBLEM TO BE SOLVED: To provide an **encapsulated** pharmaceutical preparation containing **S-adenosylmethionine** or its salts, capable of being easily taken by every body, and being expected that its medicinal effect is easily developed.

SOLUTION: This **encapsulated** pharmaceutical preparation is prepared by **encapsulating** a liquid in a **capsule** casing consisting mainly of **gelatin**, wherein the liquid is obtained by dispersing or suspending the **S-adenosylmethionine** or its salts in an oily liquid. A mixture which is obtained by adding an emulsifier and a thickener to an oil is preferably used as the oily liquid.

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